REMARKS

Applicants wish to thank Examiner Schnizer for the courtesy shown Applicant and Applicant's representative during the interview conducted February 13, 2001. Applicants appreciate the suggestions provided by the Examiner during the interview.

With entry of this amendment, Claims 1-4, 6-12, and 14-16 are pending. Claims 1, 7, 9, and 15 have been amended. Claims 5 and 13 have been canceled, and no new claims have been added. Support for the amendments to the claims can be found throughout the original specification and claims. Support for the generic name for Tween 80 is supported by pages from the Aldrich chemical catalog. No new matter has been added by these amendments.

This amendment is accompanied by a Petition for a three-month extension of time and a check in the amount of $445.00 to cover the extension fee. No additional fees are believed due. However, the Commissioner is hereby authorized to charge any deficit, or credit any overpayment, to Deposit Account No. 11-0855.

REJECTION OF CLAIMS 1-16 UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 1-16 have been rejected under 35 U.S.C. § 112, first paragraph, as nonenabling for the full scope of the invention. Particularly, the Office Action states that "while being enabling for compositions which can alter gene activity, such as are known in the art, and for intramuscular delivery and expression of nucleic acids in vivo as is known in the art, does not reasonably provide enablement for therapeutic delivery of any and all nucleic acids in vivo. "

Applicants have followed the Examiner's suggestion made during the interview conducted February 13, 2001. The claims as amended recite "a composition" and a "method for delivering a compound." Applicants assert that the amended claims fully comply with 35 U.S.C. § 112 and respectfully request reconsideration and withdrawal of this ground of rejection.

REJECTION OF CLAIMS 7 AND 15 UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 7 and 15 have been rejected under 35 U.S.C. § 112, second paragraph. Specifically, the Office Action states that "Claims 7 and 15 contain the trademark/trade name Tween 80. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. § 112, second paragraph."

Claims 7 and 15 have been amended to recite the generic name of the compound, polyoxyethylene (20) sorbitan monooleate, rather than the tradename. This amendment does not change the scope of the claim, but rather substitutes another name for the same compound. Applicants have included a page from the Aldrich chemical catalog showing the generic name for Tween 80. Applicants request the Examiner to withdraw this rejection.

REJECTION OF CLAIMS 1-4, 6, 9-12, AND 14 UNDER 35 U.S.C. § 102(B) OVER U.S. PATENT NO. 4,772,466 TO ALLISON *ET AL.*

Claims 1-4, 6, 9-12, and 14 have been rejected under 35 U.S.C. § 102(b) as anticipated by U.S. Patent No. 4,772,466 to Allison et al. Specifically, the Office Action states that "Allison teaches a composition comprising an immunologically effective amount [of] an antigen and block copolymer composed of POE and POP moieties. Preferred embodiments include a copolymer comprising a POP constituent of from 3250-4000 molecular weight, and about 10-20% (w/w) POE. The composition may also comprise 0.5%-2.5% (w/w) TWEEN 80, and 1%-30% (w/w) alcohol. The alcohol may be from 6-30 carbon atoms in length. It is noted that the range of 1-30% (w/w) overlaps the claimed range of 0.5%-5% (v/v) because the density of alcohols is slightly less than that of water. Allison also teaches a method of using the composition to cause an immune response. By definition, an immune response requires alterations in gene activity, e.g. the production of antibodies."

Applicants respectfully traverse this rejection for the following reasons. The claims as amended recite compositions that contain genes, oligonucleotides, antisense oligonucleotides, triplex DNA compounds, and/or ribozymes. Allison does not teach or

suggest the use of such compounds. Therefore, Allison does not contain each and every feature of the claims.

Further, Allison actually teaches away from the claimed invention. Allison teaches that its compositions increase immunogenicity to an antigen contained within the compositions. However, an increased host immune response is undesirable for the delivery of genetic material for use of compositions for gene therapy.

For at least these reasons, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

REJECTION OF CLAIMS 1-16 UNDER 35 U.S.C. §§ 102(E) AND (G) OVER U.S. PATENT NO. 5,567,859 TO EMANUELE ET AL.

Claims 1-16 have been rejected under 35 U.S.C. §§ 102(e) and (g) as anticipated by over U.S. Patent No. 5,567,859 to Emanuele et al. Specifically, the Office Action states that "Emanuele teaches a composition comprising a block copolymer composed of POE and POP moieties, as well as either antibiotics, or antisense oligonucleotides, triplex DNA compounds, or ribozymes. Preferred embodiments include a copolymer comprising a POP constituent of from 2250-4000 molecular weight, and about 10-30% (w/w) POE. The composition may also comprise 2% (w/w) TWEEN 80, and 1% (w/w) ethanol. It is noted that this composition, while not enabled for therapeutic use of nucleic acids, is enabled for delivery of nucleic acids *in vivo*, and for therapeutic delivery of antibiotics. Delivery of antibiotics would be expected to indirectly alter the expression of genes associated with immune response by eliminating the infectious agents."

Applicants submit that the range of poloxamers taught by the '859 Emanuele et al. patent are not coextensive with the range of poloxamers recited by the currently pending claims. Nor does the '859 Emanuele et al. patent teach the inclusion of all of the genetic material recited by the currently pending claims. Therefore, the '859 Emanuele et al. patent does not contain each and every feature of the claims.

With regard to the rejection under 35 U.S.C. § 102(g) is it noted that the '859 patent and the present application contain overlapping inventors. The subject matter of the claims, although related, is not the same. The present claims require the presence of genetic material in the composition, whereas the claims of the '859 patent do not.

For at least these reasons, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

REJECTION OF CLAIMS 1-6, 8-14, AND 16 UNDER 35 U.S.C. § 103 OVER SIMONS ET AL (NATURE, 359: 67-70, 1992), U.S. PATENT NO. 4,772,466 TO ALLISON ET AL., AND ROBINSON-BENION ET AL. (ANTISENSE RES. & DEV., 1(1): 21-33, 1991)

Claims 1-6, 8-14, and 16 have been rejected under 35 U.S.C. § 103 as obvious over Simons et al (Nature, 359: 67-70, 1992), U.S. Patent No. 4,772,466 to Allison et al., and Robinson-Benion et al. (Antisense Res. & Dev., 1(1): 21-33, 1991). Specifically, the Office Action states that "Simons teaches the delivery of antisense c-myb oligonucleotides to rat arterial smooth muscle cells by the application of a composition of antisense oligonucleotide and a block copolymer for the purpose of inhibiting gene expression and cell proliferation. Simons used Pluronic™ F-127, which as a POP molecular weight of about 4000 and is 70% POE by weight. Simons does not teach a block copolymer comprising less than 50% POE by weight, or an expression vector."

The Office Action also states that "Allison teaches a composition comprising an immunologically effective amount [of] an antigen and block copolymer composed of POE and POP moieties. Preferred embodiments include a copolymer comprising a POP constituent of from 3250-4000 molecular weight, and about 10-20% (w/w) POE. The composition may also comprise 0.5%-2.5% (w/w) TWEEN 80, and 1%-30% (w/w) alcohol. The alcohol may be from 6-30 carbon atoms in length. It is noted that the range of 1-30% (w/w) overlaps the claimed range of 0.5%-5% (v/v) because the density of alcohols is slightly less than that of water. Allison also teaches a method of using the composition to cause an immune response. By definition, an immune response requires alterations in gene activity, e.g., the production of antibodies."

Further, the Office Action states that "Robinson-Benion teaches a vector designed to express antisense RNA which suppresses the expression of c-fos, and suggests the use of this antisense inhibition to analyze the mechanism of transcriptional repression *in vivo*. It would have been obvious to substitute the block copolymer of Allison for the lock copolymer of Simons. One would have been motivated to do so because such compounds can be considered analogous or homologous. That is, they are sufficiently structurally similar that there is a presumed expectation that they will possess similar properties. It would have been similarly obvious to substitute the expression vector of Robinson-Benion for the antisense oligonucleotides of Simons et al in order to study the mechanism of c-fos transcriptional repression *in vivo*, as suggested by Robinson-Benion."

Applicants respectfully traverse this rejection for the following reasons. Simons teaches that hydrogel forming Pluronics can be used as a depot from which antisense oligonucleotides can passively diffuse. These polymers form hydrogels due to their high POE content. In contrast, the poloxamers of the claimed invention contain a much lower POE content and do not form a hydrogel like that in Simons. Simons does not teach or suggest poloxamers having a low POE content which do not form a hydrogel.

Additionally, the poloxamers described by Simons and Allison are not analogous or homologous for the following reasons. Poloxamers have very different physical and chemical properties depending upon the total size of the polymer, the size of the hydrophobic portion of the polymer, and the percent hydrophile. For example, the poloxamers of Simons contain a high POE content and thus form thermo-reversible hydrogels. The poloxamers of Allison contain a low POE content and, therefore, do not form hydrogels.

Further, one having ordinary skill in the art would not be motivated to combine the teachings of Simons and Allison because the increased immunogenicity of Allison's compositions would be detrimental to Simons' use as a drug delivery system. Robinson-Benion does not teach or suggest the use of poloxamers. Therefore, nothing in Robinson-Benion overcomes the deficiency of the combination of Simons and Allison.

For at least these reasons, Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

MARKED COPY OF AMENDMENTS

Amendments to the Claims:

1. (Twice Amended) A [therapeutic] composition for treating a human or animal comprising,

[a compound capable of altering nucleic acid function for altering gene activity] one or more genes, oligonucleotides, antisense oligonucleotides, triplex DNA compounds, or ribozymes admixed with a nonionic block copolymer, wherein the block copolymer has the following formula:

$$HO(C_2H_4O)_b(C_3H_6O)_a(C_2H_4O)_bH$$

wherein the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 750 and 15,000 and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between is approximately 1% and less than 50% of the copolymer.

7. (Amended) The composition of Claim 6 wherein the surfactant is [Tween 80] polyoxyethylene (20) sorbitan monooleate and the alcohol is ethanol.

9. (Twice Amended) A method of delivering a compound for altering gene activity to a human or animal comprising,

[the step of]administering to a human or animal a composition comprising [a compound for altering gene activity] <u>one or more genes, oligonucleotides, antisense oligonucleotides, triplex DNA compounds, or ribozymes</u> admixed with a nonionic block copolymer, wherein the block copolymer has the following formula:

$$HO(C_2H_4O)_b(C_3H_6O)_a(C_2H_4O)_bH$$

wherein the molecular weight represented by the polyoxypropylene portion of the copolymer is between approximately 750 and 15,000 and the molecular weight represented by the polyoxyethylene portion of the copolymer constitutes between is approximately 1% and less than 50% of the copolymer.

15. (Amended) The method of Claim 14 wherein the surfactant is [Tween 80] <u>polyoxyethylene (20) sorbitan monooleate</u> and the alcohol is ethanol.

CLOSING

Applicants respectfully submit that this is a complete response to the Office Action dated November 21, 2000, and that Claims 1-4, 6-12, and 14-16 are patentable. Early and favorable consideration is earnestly solicited. If the Examiner believes there are other issues that can be resolved by telephone interview, or that there are any informalities remaining in the application which may be corrected by Examiner's Amendment, a telephone call to the undersigned attorney at (404) 949-2400 is respectfully solicited.

Respectfully submitted,

KILPATRICK STOCKTON, LLP

By: Mary Anthony Merchant, Ph.D.
Reg. No. 39,771

KILPATRICK STOCKTON, LLP
2400 Monarch Tower
3424 Peachtree Road, N.E.
Atlanta, GA 30326
Phone: (404) 949-2400
Fax: (404) 949-2499
Atty Docket: 19720-0624
KS#: 42896-216422